UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS
EASTERN DIVISION

PHARMASTEM THERAPEUTICS, INC., a Delaware corporation, Plaintiff, v. VIACELL, INC., a Delaware corporation, OBSTETRICAL AND GYNECOLOGICAL ASSOCIATES, P.A., and FEMPARTNERS, INC., a Delaware corporation, Defendants.	Civil Action No.: 04-CV-11673-RWZ

PLAINTIFF'S MEMORANDUM IN SUPPORT OF ITS MOTION FOR A PRELIMINARY INJUNCTION AGAINST VIACELL, INC.

Plaintiff PharmaStem Therapeutics, Inc. seeks to preliminarily enjoin defendant ViaCell, Inc. from infringement of PharmaStem's U.S. Patent Nos. 6,461,645 B1 (the "'645 Patent") and 6,569,427 B1 (the "'427 Patent")(collectively, the "Patents-In-Suit"). 35 U.S.C. § 283.[1]

BACKGROUND

PharmaStem is the owner of a pioneering invention that indisputably changed the world of hematopoietic stem cell transplantation by fundamentally adding to the universe of available therapies for cancer and other diseases and disorders. The Patents-In-Suit are generally directed toward therapeutic compositions of fetal or neonatal hematopoietic stem and progenitor cells of the blood derived from the umbilical cord or placenta of a newborn at birth ("cord blood"), and methods of isolating, preserving, and using such compositions. The principal value of cord blood lies in its capacity to reconstitute hematopoietic, or blood and immune, systems damaged by diseases or disorders.

[1] *See* Declaration of Edward W. Little ("Little Decl."), Exhs. 1, 2.

The inventors discovered that the blood in the umbilical cord and placenta of a newborn contained stem cells that, despite the relatively tiny amount of cord blood available from a single newborn, could be a valuable medical resource for persons in need of hematopoietic stem cell transplants. *See* '645 Patent at col. 11:55 to 12:35; '427 Patent at col. 13:32 to col. 14:11. In September 1988, the inventors directed a clinical trial, collecting, cryopreserving, and providing the cord blood, for the world's first successful cord blood stem cell transplant. *See* '645 Patent at col. 57:1 to col. 58:67; '427 Patent at col. 56:63 to col. 58:7. Until the discovery of the therapeutic utility of cord blood by the PharmaStem inventors, the primary treatment option for a patient requiring a hematopoietic stem cell transplant was bone marrow transplantation, while the potentially life-saving cord blood was routinely discarded as medical waste. With the advent of cord blood transplantation, cord blood could be easily preserved for possible future use by the donor, a family member, or sufficiently-matched unrelated patients. PharmaStem's pioneering work is, today, roundly acknowledged by the scientific and medical communities.[2]

PharmaStem (f/k/a Biocyte), established in 1985, pioneered the industry of private cord blood banking. Its earliest imitators and competitors, including ViaCell, did not come onto the scene until years later.[3] As ViaCell's business plans describe, only two years after the first of PharmaStem's cord blood banking patents—U.S. Patent No. 5,004,681 B1 ("'681 Patent")—issued, one competitor requested reexamination. With the senior-most patent in reexam untl 2000, ViaCell seized its chance to build an infringing business. ViaCell has grown to become a large and profitable private cord blood bank.[4]

Presciently, in its '93/'94 business plans, ViaCell stated:

> "Biocyte has two patents on cord blood. They have patented the cryopreservation and therapeutic use of hematopoietic stem and progenitor cells derived from umbilical cord and placental blood. These patents are currently in reexamination by the U.S. Patent office… The

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[2] *See*, *e.g.*, Little Decl., Exhs. 3 (BBC Documentary), 22 (Gluckman medical journal article at 1197), 27 (Koh medical journal article at 1).

[3] *See* Little Decl., Exh. 4; *see also* Little Decl., Exh. 5 at 1448:2-1450:22 (ViaCell's Founder, Cynthia Fisher, authenticating contents of the ViaCell Business Plan as "provid[ing] full disclosure").

[4] *See* Little Decl., Exh. 6.

patents they hold are broad and in question due to prior art in the field. They have been in reexamination since October, 1993. ***The patents are a known and acknowledged risks [sic]. The verdict will play a role in the outcome and success of this business opportunity.***

"We view Biocyte as our strongest competitor. ***The founding scientists are core researchers in this field*** and have published many related articles. Biocyte's time, energies, and financial resources have been spent doing much education and development in this field. ***They are the trailblazers. Cross country skiing behind the trail blazer conserves energy and resources.***[5]

Simply put, ViaCell has "skied" in PharmaStem's trail long enough, earning a windfall practicing another's invention in total disregard of the other's patent rights.

There can be little question that ViaCell, a private cord blood bank that collects, cryopreserves, and stores newborns' cord blood for future therapeutic use by the donors or their family members, runs an infringing business. As demonstrated herein, ViaCell's own public and private statements, practices, and cord blood banking activities, in addition to the overwhelming scientific evidence, firmly establish that ViaCell's stored cord blood units directly infringe every relevant claim limitation of the Patents-In-Suit. Accordingly, and because PharmaStem will suffer irreparable harm absent an injunction, the balance of hardships tips in PharmaStem's favor, and the public interest favors an injunction, the Court should issue the injunction.

ARGUMENT

I. PHARMASTEM IS ENTITLED TO PRELIMINARY INJUNCTIVE RELIEF AGAINST VIACELL'S INFRINGEMENT OF THE PATENTS-IN-SUIT.

35 U.S.C. § 283 expressly authorizes trial courts to grant preliminary injunctive relief in patent infringement cases. 35 U.S.C. § 283 ("The several courts having jurisdiction of cases under this title may grant injunctions in accordance with the principles of equity to prevent the violation of any right secured by patent, on such terms as the court deems reasonable."); *see Oakley, Inc. v. Sunglasses Hut Int'l*, 316 F.3d 1331, 1338-39 (Fed. Cir. 2003); *see also Hybritech, Inc. v. Abbot Labs.*, 849 F.2d 1446, 1456-57 (Fed. Cir. 1988)("The patent statute provides injunctive relief to preserve the legal interest of the parties against future infringement which may have market effects never fully compensable in money.").

[5] *See* Little Decl., Exh. 4 at page 1 (emphasis added).

PharmaStem "is entitled to a preliminary injunction if it shows the following four factors: (1) a reasonable likelihood of success on the merits; (2) irreparable harm absent an injunction; (3) that the balance of hardships tips in its favor; and (4) that the public interest favors an injunction." *Tate*, 279 F.3d at 1364-65 (citations omitted). "In order to demonstrate likely success on the merits, [PharmaStem] must show that, in light of the presumptions and burdens applicable at trial, it will likely prove that [ViaCell] infringes the asserted claims of the [Patents-In-Suit] and that the patent[s] will likely withstand [ViaCell's] challenges to [their] validity." *Id.* at 1365 (citations omitted).

Lastly, the proof required for the grant of a preliminary injunction is "no more nor less stringent in patent cases than in other areas of law." *See H.H. Robertson Co. v. United Steel Deck, Inc.*, 820 F.2d 384, 387 (Fed. Cir. 1987), *overruled on other grounds by, Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 977 (Fed. Cir. 1995). In the case of proving patent infringement, PharmaStem's burden of proof is by a preponderance of the evidence. *Hughes Aircraft Co. v. United States,* 717 F.2d 1351, 1361 (Fed. Cir. 1983). Moreover, at the preliminary-injunction stage, a party is not required to prove his case in full and the findings of fact and conclusions of law made by a court granting a preliminary injunction are not binding at trial on the merits. *Univ. of Tex. v. Camenisch*, 451 U.S. 390, 395 (1981).

II. THERE IS A REASONABLE LIKELIHOOD OF SUCCESS ON THE MERITS OF PHARMASTEM'S PATENT INFRINGEMENT CLAIMS AGAINST VIACELL.

A. ViaCell's Cord Blood Banking Activities Infringe the Patents-In-Suit.

"An assessment of the likelihood of infringement, like a determination of patent infringement at a later stage in litigation, requires a two-step analysis. First, the court determines the scope and meaning of the patent claims asserted ... [Secondly,] the properly construed claims are compared to the allegedly infringing device." *Oakley*, at 1339 (internal quotations omitted), citing, *Cybor Corp. v. FAS Techs., Inc.,* 138 F.3d 1448, 1454 (Fed. Cir. 1998)(en banc)(citations

omitted).[6] "Step two, comparison of the claim to the accused device, requires a determination that every claim limitation or its equivalent be found in the accused device." *Id.* at 1339, citing, *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.,* 520 U.S. 17, 29 (1997).

1. PharmaStem's Proposed Claim Construction.

A patent's scope is determined by its claims. *Digital Biometrics Inc. v. Identix*, *Inc.*, 149 F.3d 1335, 1344 (Fed. Cir. 1998). The interpretation of claim language is a matter of law, and is thus reserved exclusively for the Court. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 372 (1996). In construing the claims, the Court is to ascertain the meaning they would have for one of ordinary skill in the art who had read the patent's disclosure and public record—the claims, the specification, and the prosecution history. *Markman*, 517 U.S. at 370; *Loctite Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 867 (Fed. Cir. 1985). This public record constitutes the "intrinsic evidence" from which the patent's scope must be discerned. *Vitronics Corp. v. Conceptronic Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). Claim terms are to be accorded their ordinary and accustomed meaning unless they lack such ordinary meaning, or unless the context makes clear that some other meaning should apply. *Johnson Worldwide Associates, Inc. v. Zebco Corp.*, 175 F.3d 985, 989 (Fed. Cir. 1999).

PharmaStem anticipates that it will assert, at least, the Claim 17 of the '645 Patent and Claims 46 and 49 of the '427 Patent in this litigation, and proposes the following construction for the claim terms.

Claim Language	PharmaStem's Proposed Construction
hematopoietic stem cells	PROPOSED CONSTRUCTION: cells capable of effecting repopulation of blood and other hematopoietic organs.
in an amount sufficient to effect hematopoietic reconstitution of a human adult,	This claim term requires no construction. If the term "in an amount sufficient" or the term "hematopoietic reconstitution" requires construction, then PharmaStem proposes the following construction. PROPOSED CONSTRUCTION: in an amount that is as much as is needed to effect repopulation of a human adult's blood and other

[6] PharmaStem's proposed claim construction is supported by the evidence set forth in the claim charts at Appendix A to this motion. For the Court's convenience, infringement charts are set forth at Appendix B.

	hematopoietic organs.
cryopreserved	This claim term requires no construction. If the term "cryopreserved" requires construction, then PharmaStem offers the following construction. PROPOSED CONSTRUCTION: stored at very low temperatures.
pharmaceutically acceptable carrier.	This claim term requires no construction. If the term "pharmaceutically acceptable carrier" requires construction, then PharmaStem offers the following construction. PROPOSED CONSTRUCTION: any medically acceptable carrier, including but not limited to saline, buffered saline, dextrose and water.

Most of the claim terms do not require any construction other than their plain and ordinary meaning. Nor does PharmaStem anticipate that many of the proposed claim constructions will be disputed, because the same terms have been previously construed in a prior litigation between PharmaStem and ViaCell, among others, involving related patents.[7] *See Mycogen Plant Science, Inc. v. Monsanto Co.,* 252 F.3d 1306, 1310-12 (Fed. Cir. 2001)(the terms of the claims of related patents construed in one action should be construed consistently in subsequent actions), *vacated on other grounds* by *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.,* 535 U.S. 722 (2002).

2. ViaCell's Cord Blood Units ("CBUs") Meet Every Limitation of Claim 17 of the'645 Patent.

As ViaCell itself states, "Viacord was established in 1993 to give expectant parents an opportunity to bank their children's cord blood with comfort and security. Prior to launching our Cord Blood Banking Service, Viacord conducted extensive research and validation studies to ensure that we set the highest standards regarding the collection, processing, and storage of cord

[7] For example, in the prior litigation, the entire phrase "[hematopoietic stem cells] in an amount sufficient to effect hematopoietic reconstitution of a human adult" was construed to mean "present in an amount that is as much as is needed to effect hematopoietic reconstitution of a human adult."[7] As can be seen from the prior claim construction, the term "in an amount sufficient" was given its plain meaning, while the term "hematopoietic reconstitution" was not construed at all. Therefore, if construction is required, "in an amount sufficient to effect hematopoietic reconstitution of a human adult" should be construed as "present in an amount that is as much as is needed to effect hematopoietic reconstitution of a human adult," consistent with the prior claim construction.

blood."[8] Viacord's self-proclaimed mission is "[t]o provide the highest quality stem cell preservation service and care to our patients, families and their physicians. We at Viacord believe these words are much more than just a promise. They are the commitment we live by."[9] Accordingly, ViaCell's "Viacord Enrollment Agreement," available on its website, states under its "Terms and Conditions" that "Viacord's Cord Blood Banking Service [] provides for the collection materials, testing, processing, cryopreservation and storage of the cells that remain in the placenta and umbilical cord after the birth of your child."[10] It should, therefore, be of little surprise to find that ViaCell practices the patents which pioneered the industry in which it operates.

a. ViaCell's CBUs comprise "viable human neonatal or fetal hematopoietic stem cells derived from the umbilical cord or placental blood of a single human collected at the birth of said human, which have been cryopreserved."

The following excerpts from ViaCell's website constitute just some of the overwhelming evidence that ViaCell's CBUs meet the above claim limitations. ViaCell's CBUs are pharmaceutical compositions comprising ***human neonatal or fetal hematopoietic stem cells derived from the umbilical cord or placental blood of a single human collected at the birth of said human***, which are ***cryopreserved***:

- "In the early 1980s, Dr. Hal Broxmeyer (now a member of Viacord's Medical Scientific Advisory Board) was instrumental in validating that the blood remaining in the umbilical cord after birth is rich in a precious resource called stem cells. Stem cells are the building blocks of our blood and immune systems and, potentially, the nervous system, skin, bones, heart, endocrine organs and other body tissue. Over the past decade, thousands of cord blood stem cell transplants have been successfully performed worldwide."[11]

- "Your pregnancy provides an opportunity to do something extraordinary for your baby and your entire family. By choosing to preserve your newborn's cord blood with Viacord, you will preserve your family's chance to potentially use it as part of a treatment therapy for over

[8] *See* Little Decl., Exh. 8, at page 1.
[9] *See* Little Decl., Exh. 8, at page 1.
[10] *See* Little Decl., Exh. 9, at § 1.
[11] *See* Little Decl., Exh. 10.

40 diseases, including various cancers, genetic diseases, blood disorders and immune system deficiencies."[12]

- "(Step 1:) Once you have enrolled, you will receive a collection kit to take with you to the hospital when you are ready to deliver. We will also provide your doctor with the materials and training needed for the cord blood collection. (Step 2:) Upon arriving at the hospital, give Viacord's 24-hour on-call service a call so we can review the collection process with your doctor or nurse. . . (Step 3:) After delivering your newborn, your doctor clamps and cuts the umbilical cord then takes your baby out of the birthing area. The collection itself is simple, aseptic, painless and does not interfere with your delivery. . . (Step 4:) Once you've called Viacord to let us know the cord blood was collected, Viacord arranges for a private medical courier to bring your baby's cord blood unit to the nearest airport where it is put on the next flight out to our state-of-the-art long-term storage facility. . . (Step 5:) Upon receipt of your baby's cord blood unit our storage facility conducts the following tests on the cord blood sample that are essential in the event of a potential transplant: the volume collected, the number and viability of nucleated cells, sterility, and the percent of CD34 cells. . . (Step 6:) After testing, your baby's cord blood unit is cryopreserved in cryoprotected blood bags at -196 degrees Celsius (-321 degrees Fahrenheit). . ."[13]

- "In the event that your cord blood unit is needed for transplant, Viacord will conduct appropriate testing on both the cord and maternal blood samples and ship the cord blood unit to the appropriate facility upon written request from a physician qualified to perform a stem cell transplant."[14]

ViaCell's CBUs comprise ***viable*** cord blood stem cells:

- "**How long can cord blood stem cells be stored?** Scientific research has yet to determine the actual length of time these cells can be stored and still be viable. It is known that cord blood stem cells remain viable for many years and possibly decades. So far, the longest time bone marrow stem cells have been frozen and successfully transplanted was eleven years as reported by Dr. Joe Antin in Bone Marrow Transplantation in 1992. Dr. Peter Kobylka of the University of Amsterdam showed viability of cord blood stem cells frozen for 15 years."[15]

b. ViaCell's CBUs comprise hematopoietic stem cells "in an amount sufficient to effect hematopoietic reconstitution of a human adult."

In addition to the evidence adduced above, the following excerpts from ViaCell's website constitute just some of the overwhelming evidence that ViaCell's CBUs comprise ***a sufficient amount of hematopoietic stem cells to effect hematopoietic reconstitution of a human adult***.

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[12] *See* Little Decl., Exh. 11.
[13] *See* Little Decl., Exh. 12, *passim*.
[14] *See* Little Decl., Exh. 9, at § 1.
[15] *See* Little Decl., Exh. 13, at page 3.

(Notably, there is no actual requirement in Claim 17 of the '645 Patent that the CBU must reconstitute an adult, if used, but merely that there be enough stem cells to do so.)

ViaCell's Own Admission and Representations:

- **"Your baby's cord blood could someday save a life. Your baby's. Your family's. Yours."**[16]

- "Cord blood stem cells are a perfect match for your baby, have a high probability of being a viable match for a sibling and can be potentially be used for parents and grandparents in the treatment of over 40 diseases including a wide range of cancers, genetic diseases, immune system deficiencies and blood disorders."[17]

- "Umbilical cord blood offers a perfectly natural, controversy-free method of acquiring stem cells. (Even the Pope approves of cord blood banking.) Cord blood offers several advantages over other methods. It's collected in a safe, 5-minute procedure after a baby is born and is painless for both mother and baby. Also, cord blood transplants have a significantly lower rate of graft vs. host disease than bone marrow transplants. Plus, cord blood stem cells are a perfect match for the baby and can potentially be used to treat siblings and other family members as well. . . In April of 1995, a 32-year-old man from the Netherlands received the most precious gift of all from his newborn daughter. It was the gift of life. After years of continuous struggle with leukemia, the young father preserved his newborn's cord blood stem cells, which in turn were used to treat his life- threatening disease. This was perhaps one of the most extraordinary gifts ever exchanged between a father and a daughter. Not to mention, a true testament of the power of cord blood."[18]

- "**How many samples have been used for transplant from Viacord? Did they all engraft?** Eleven of our banked units have been used in transplant—all have successfully engrafted."[19]

- "**What is the process once the blood center receives my child's cord blood unit?** Upon receipt of your baby's cord blood unit, our lab conducts a battery of tests . . . We'll give you the volume collected and the counts of nucleated cells which are the most critical to successful engraftment."[20]

- "**What needs to be done to retrieve the sample?** If your sample is ever needed, just notify Viacord. We will ask you to sign a release form and indicate the name and address of the hospital where your unit will be going. Then Viacord and the other hospital will work out the details for immediate transfer."[21]

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[16] *See* Little Decl., Exh. 14.
[17] *See* Little Decl., Exh. 14.
[18] *See* Little Decl., Exh. 15.
[19] *See* Little Decl., Exh. 16, at page 3.
[20] *See* Little Decl., Exh. 13, at page 1.
[21] *See* Little Decl., Exh. 17, at page 1.

However, perhaps the best evidence that ViaCell uses, stores and offers to store cord blood units containing hematopoietic stem cells in an amount that is as much as is needed to effect repopulation of a human adult's blood and other hematopoietic organs, lies in its "**Quality Product Guarantee**." ViaCell guarantees the following: "If the cord blood stem cells processed and stored by Viacord are used in a hematopoietic stem cell transplant following standard, recognized medical practices and they do not engraft, Viacord will pay $25,000 to the legal owner of the cells per the Viacord Enrollment Agreement."[22] Notably, ViaCell's guarantee explicitly includes transplants to the biological parents of the donor, so long as, the transplanted cord blood does not contain less than 2×10^7 total nucleated cells per kilogram or less than 1×10^5 CD34+ cells per kilogram, is not co-transplanted with supplemental stem cell sources (*e.g.*, additional cord blood, peripheral blood or bone marrow), and does not use experimental procedures, such as, stem cell expansion.[23] Thus, so long as the adult patient is a biological parent of the donor and the transplanted cord blood contains at least 2×10^7 total nucleated cells per kilogram and 1×10^5 CD34+ cells per kilogram, ViaCell guarantees hematopoietic reconstitution.

The Scientific Evidence:

Additionally, overwhelming scientific evidence exists to support ViaCell's storage and offer to store cord blood units containing hematopoietic stem cells in an amount that is as much as is needed to effect repopulation of a human adult's blood and other hematopoietic organs. As a preliminary matter, the '645 Patent and the '427 Patent, themselves, disclose that "[i]n a preferred embodiment, volumes of 50 ml or more of neonatal blood are obtained," citing information that "suggests that as little as 50 ml of cord blood contains enough of the appropriate cells to repopulate the hematopoietic system of an adult, and it is possible that even less cord blood would have the same effect." '645 Patent at col. 11:55 to col. 12:20; '427 Patent at col. 13:32-45. Importantly, what is claimed is "an amount sufficient," and not the preferred

[22] *See* Little Decl., Exh. 9, at last two pages.
[23] *See* Little Decl., Exh. 9, at last page.

embodiment, *i.e.*, approximately 50 ml. To that end, the current scientific and medical consensus is that a typical cord blood collection is of sufficient size for use in almost all transplant conditions, regardless of patient age. Thus, all, or almost all, of ViaCell's CBUs are reasonable likely to be sufficient to effect repopulation of a human adult's blood and other hematopoietic organs. In addition to the evidence adduced above, the following excerpts from the scientific evidence constitute just some of the overwhelming evidence that ViaCell's CBUs meet the above claim limitation.

- Harris, D. T., *Cord Blood Banking and Its Potential Clinical Applications*.[24]

As early as 1995, Dr. David T. Harris, currently a medical and scientific advisor to fellow private cord blood bank CBR Systems, Inc., already observed that "questions have been raised as to whether cord blood transplantation would ever be suitable for adult use, or restricted to use in children. To date, the smallest amount of cord blood ever used in a successful transplant has been 43 cc, and the largest patient ever successfully transplanted is now 85 kg. ***Thus, it appears that a typical cord blood collection is of sufficient size for use in almost all transplant conditions.***" At page 3 (emphasis added).

- Laughlin, M. J., *et al.*, *Hematopoietic Engraftment And Survival In Adult Recipients Of Umbilical-Cord Blood From Unrelated Donors*, New England Journal of Medicine (2001)("Laughlin").[25]

The Laughlin study, published in 2001, was one of the first large-scale, multi-center studies to conclude that cord blood contains a sufficient number of stem cells to reconstitute an adult. In brief, the Laughlin study spanned five years, from 1995 to 2000, and tracked the health of 68 adult patients with life-threatening blood disorders who received transplants of cord blood from unrelated donors. At 1815-16. The subject patients ranged from 17 to 58 years of age, and ranged in weight from 40.9 kg to 115.5 kg, at the time of transplantation. At 1817.

[24] *See* Little Decl., Exh. 18.
[25] *See* Little Decl., Exh. 19.

The purpose of this study was to determine whether cord blood contained stem cells in an amount sufficient to reconstitute an adult. The results demonstrated that approximately 90% of the subject patients achieved hematopoietic recovery. At 1817. Furthermore, the study found no correlation between cell dose and speed of hematopoietic recovery, where the cell doses ranged from 10 million to 63 million nucleated cells per kilogram of the recipient's body weight. At 1816-18.

> Accordingly, the Laughlin study concluded:
> "***In summary, the results of this study demonstrate that HLA-mismatched umbilical-cord blood from unrelated donors is a feasible alternative source of hematopoietic stem cells for transplantation in adults.*** Hematopoietic reconstitution occurred in 90 percent of our patients, and the incidence and severity of GVHD were low despite HLA mismatching." At 1821 (emphasis added).

The Laughlin study is a powerful testament to the capability of the cord blood from a single newborn donor to repopulate the entire hematopoietic system of a needy adult patient. At 1818. Whereas "[r]apid engraftment of marrow from siblings and unrelated donors is related to the dose of cells, the number of CD34+ cells, and the degree of HLA matching," the Laughlin study found that the same correlations did not hold true with respect to cord blood stem cell transplantation. At 1819-20. Thus, even relatively small cord blood units are highly likely to contain stem cells in an amount sufficient to effect hematopoietic reconstitution.

- *Umbilical Cord Stem Cell Transplants Should Not Be Limited By Age*, The Blue Sheet (Food and Drug Administration), March 5, 2003 ("FDA Blue Sheet").[26]

In 2003, the FDA's Biological Response Modifiers Advisory Committee ("Advisory Committee") agreed that "[p]lacental ***cord blood transplant recipient age should not be a factor***." At 21 (emphasis added). Notably, "the committee did not want to put a firm figure on minimum or maximum cell doses…" *Id.* The Advisory Committee's determination, not only sets forth the most reliable indicator of the current state of the art, but also underscores the importance of the Laughlin study's finding that there was no correlation between cell dose, once a threshold amount is present, and the speed of hematopoietic recovery.

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[26] *See* Little Decl., Exh. 20.

Further similar scientific evidence is summarized below:

Sanz, G. F., *et al.*, *Standarized, Unrelated Donor Cord Blood Transplantation in Adults with Hematologic Malignancies*, Blood (2001)("Sanz").[27] Sanz reported the results of cord blood transplantation in 22 adult patients, ranging in age from 18 to 46 years, and weight from 41 to 85 kilograms. This study also concluded that there are sufficient amounts of stem cells in cord blood, as over 90% of the adult patients experienced engraftment. Sanz determined that cord blood transplantation, "despite the low cellular dose infused, is capable of promoting sustained hematopoietic engraftment in most adult recipients." At 2337.
Gluckman. E., *Current Status of Umbilical Cord Blood Hematopoietic Stem Cell Transplantation*, Experimental Hematology (2000)("Gluckman").[28] Gluckman reported the outcomes of 108 adult patients who received cord blood transplants in Europe. The adult patients ranged in age from 15 to 53, and weighed in the range of 35 to 110 kilograms. This report demonstrated that over 80% of the adult patients attained engraftment from the cord blood stem cells. The "results show that [cord blood transplantation] can be a good option for adults." At 1202.
Iseki, T., *et al., Unrelated Cord Blood Transplantation in Adults with Hematological Malignancy: A Single Institution Experience*, Blood Abstract #2789 (2000)("Iseki").[29] Iseki reported the results of cord blood transplantation in adults from one of the largest transplant centers outside of North America and Europe. The adults in this Japanese study had a median age and weight of 38 years and 52 kilograms, respectively. The results reported indicated that cord blood transplantation in adults "was comparable to that of standard bone marrow transplantation." At 665a.
Ooi, J., *et al., Unrelated Cord Blood Transplantation for Adults Patients with Advanced Myelodysplastic Syndrome*, Blood (2003)("Ooi I").[30] The Ooi I study reported the outcome of 13 adult patients, ranging in age from 21 to 50 years and weight from 43 to 68 kilograms, that were transplanted with cord blood stem cells. The results, *i.e.*, greater than 90% engraftment, support the finding that adult patients "should be considered candidates for [cord blood transplantations]." At 4713.
Ooi, J., *et al., Unrelated Cord Blood Transplantation for Adults Patients with De Novo Acute Myeloid Leukemia*, Blood (2004)("Ooi II").[31] Another article from Ooi *et al*., the Ooi II study, published a year after the Ooi I study, reported the outcome of cord blood transplantation in 18 adult patients. The adult patients ranged in age from 21 to 52 years, and in weight from 36.2 to 76.2 kilograms. The results from the study, *i.e.*, approximately 90% engraftment, were consistent with the previous report from Ooi *et al*., and further support the use of cord blood stem cells in adult transplantation.
Long, G. D., *et al., Unrelated Cord Blood Transplantation in Adults Patients*, Biology of Blood and Marrow Transplantation (2003)("Long").[32] Long reported the results of cord blood transplantation in 57 adult patients ranging in age from 18 to 58, and in weight from 46 to 110 kilograms. The number of successful transplantations "demonstrated that rescue with unrelated

[27] *See* Little Decl., Exh. 21.
[28] *See* Little Decl., Exh. 22.
[29] *See* Little Decl., Exh. 23.
[30] *See* Little Decl., Exh. 24.
[31] *See* Little Decl., Exh. 25.
[32] *See* Little Decl., Exh. 26.

mismatched umbilical cord blood after myeloablative therapy in adults is feasible and results in long-term engraftment." At 779. "These results suggest that unrelated umbilical cord blood transplantation is a viable option for adult patients." At 772.
Koh, L-P, *et al., Umbilical Cord Blood Transplantation in Adults Using Myeloablative and Nonmyeloablative Preparative Regimens*, Biology of Blood and Marrow Transplantation (2004)("Koh").[33] Koh, *et al.*, surveyed and reviewed several studies that have been conducted with cord blood transplantations in adult patients. As stated in Koh: "The concern of limited doses leading to a higher risk of primary graft failure in adults is related to the disproportionate difference between the number of nucleated cells in the [umbilical cord blood] graft and the adult body weight, giving rise to relative fewer infused cells per kilogram of the recipient body weight, especially in heavier patients. However, the available data on adult recipients of unrelated [umbilical cord blood transplants] thus far have shown the [umbilical cord blood] contained sufficient numbers of hematopoietic stem cells to achieve engraftment." At 6. Thus, Koh concluded that "[umbilical cord blood] contained a ***sufficient number*** of hematopoietic stem cells" to achieve engraftment in adult patients. At 9 (emphasis added).
Moscardo, F., *et al., Unrelated-Donor Cord Blood Transplantation for Adult Hematological Malignancies*, Leukemia & Lymphoma (2004)("Moscardo").[34] Moscardo reported that "the low number of hematopoietic progenitor cells present in a [umbilical cord blood] unit compared to bone marrow and peripheral blood has clearly limited the use of [cord blood transplant] in adult patients, primarily due to significant concerns about engraftment." At 11. However, since the first adult transplant in 1996, almost 30% of unrelated-donor cord blood transplants have been performed in adult patients. *Id.* Moreover, "[t]he reported data show that, contrary to initial concerns, [cord blood transplants] can promote engraftment in the majority of adult patients." At 16.
Barker, J. N., *et al., Rapid and Complete Donor Chimerism in Adult Recipients of Unrelated Donor Umbilical Cord Blood Transplantation After Reduced-Intensity Conditioning*, Blood (2003)("Barker").[35] The Barker study involved 43 adults (median age 49.5 years) transplanted with cord blood stem cells after a reduced-intensity conditioning regimen. The "data demonstrates that 0-2 antigen mismatched [umbilical cord blood] is sufficient to engraft most adults after reduced-intensity conditioning." At 1915.

c. ViaCell's CBUs also comprise "a pharmaceutically acceptable carrier," thus meeting every limitation of Claim 17 of the '465 Patent.

As described by the '645 Patent, "a pharmaceutically acceptable carrier" is broadly defined as "any sterile biocompatible pharmaceutical carrier, including but not limited to saline, buffered saline, dextrose and water." '645 Patent at col. 24:14-19. The '645 Patent discusses various techniques that involve the addition or use of various substances for various purposes

[33] *See* Little Decl., Exh. 27.
[34] *See* Little Decl., Exh. 28.
[35] *See* Little Decl., Exh. 29.

ancillary to ultimate purpose of the invention. For example, the '645 Patent describes the use of various anticoagulants well-known in the art that, though not necessary, may be helpful. '645 Patent at col. 11:27-41. The anticoagulants discussed include but are not limited to CPD (citrate-phosphate-dextrose), ACD (acid citrate-dextrose), various solutions, glucose mixtures, and heparin. *Id.* The '645 Patent also describes the use of cryoprotective agents well-known in the art that, though not necessary, may be helpful. The cryoprotectants discussed include but are not limited to dimethyl sulfoxide (DMSO), polyethylene glycol, albumin, dextran, sucrose, and ethylene glycol. '645 Patent at col. 20:24-51. The use of any of the above-described substances would satisfy the "pharmaceutically acceptable carrier" claim limitation.

Indeed, with respect to the use of DMSO, the '645 Patent teaches that the "[a]ddition of plasma (*e.g.*, to a concentration of 20-25%) can augment the protective effect of DMSO." *Id.* To that end, the '645 Patent further teaches that "[i]f desired, autologous plasma can be removed for use in the freezing process." '645 patent at col. 17:35-36. Thus, even plasma from the cord blood sample itself can also constitute a pharmaceutically acceptable carrier. Accordingly, the use of any of the substances described above, or others disclosed in the '645 Patent, or others not described, would satisfy the "pharmaceutically acceptable carrier" claim limitation.

While ViaCell most likely uses anticoagulants, the use of which will likely be discovered, at the very least, it is known that ViaCell (1) adjusts the volume of its cord blood units with plasma if the pre-processing weight is less than 45 grams and (2) always uses the cryoprotectant DMSO, diluted to 10%, and a cell media called RPMI, diluted to 10%.[36] Thus, ViaCell's CBUs indisputably meet the above claim limitation. In summary, all of the above evidence strongly shows that ViaCell offers cord blood banking services which infringe at least Claim 17 of the '645 Patent, and that PharmaStem is reasonably likely, of not more than reasonably likely, to succeed on the merits at trial.

3. ViaCell's CBUs Meet Every Limitation of Claim 46 of the'427 Patent.

[36] *See* Little Decl., Exh. 30, at page 2.

Claim 46 of the '427 Patent lacks the suitability for adult use limitation present in Claim 17 of the '645 Patent, requires "introducing into the human patient," which is absent from Claim 17 of the '645 Patent, but otherwise has the same claim limitations as Claim 17 of the '645 Patent. Accordingly, the same evidence as that adduced above clearly shows that ViaCell has induced the infringement of this claim at least eleven times in the past, by providing eleven CBUs for transplantation, or introduction into a human patient, and is imminently likely to do so again in the future.[37] *See* 35 U.S.C. § 271.

PharmaStem submits this particular evidence and argument in support of its need for some measure of preliminary injunctive relief against ViaCell.[38] As discussed in greater detail below, PharmaStem merely seeks to prevent ViaCell from rapidly gaining ***new*** clients and market share in an infringing manner, to the detriment of PharmaStem and its existing licensees.

4. ViaCell's CBUs Meet Every Limitation of Claim 49 of the'427 Patent.

Claim 49 of the '427 Patent lacks the "pharmaceutically acceptable carrier" limitation of Claim 17 of the '645 Patent, but otherwise has the same claim limitations as Claim 17 of the '645 Patent. Accordingly, the same evidence as that adduced above clearly shows that ViaCell reasonably likely also infringes this claim of the '427 Patent.

B. The Patents-In-Suit will Reasonably Likely Withstand the Defendants' Challenges to their Validity and Enforceability.

"An assessment of the likelihood of validity of a patent claim over the prior art also involves a two-step process. The first step is the same claim construction implicated in an infringement analysis." *Oakley*, at 1339, citing, *Smiths Indus. Med. Sys., Inc. v. Vital Signs, Inc.,* 183 F.3d 1347, 1353 (Fed. Cir. 1999). "The second step involves a comparison of the asserted claims with the prior art." *Id.*, citing, *Celeritas Techs. Inc. v. Rockwell Int'l Corp.,* 150 F.3d

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[37] *See, e.g.,* Little Decl., Exh. 16, at page 3.

[38] Despite ViaCell's clear likelihood of inducing infringement of at least Claim 46 of the '427 Patent, PharmaStem does not desire to hinder the provision of a cord blood unit to potentially needy patients. PharmaStem is willing to tailor any injunction to permit ViaCell to continue to provide ***existing*** CBUs to clients on demand. PharmaStem respectfully submits that such a course of action should further tip the balance in favor of granting PharmaStem the limited preliminary injunctive relief it seeks.

1354, 1360 (Fed. Cir. 1998). "Because an issued patent is presumed to be valid, 35 U.S.C. § 282, the evidentiary burden to show facts supporting a conclusion of invalidity is clear and convincing evidence, *WMS Gaming Inc. v. Int'l Game Tech.,* 184 F.3d 1339, 1355 [] (Fed. Cir. 1999)." *Id.*

At this stage of the proceedings, the Patents-In-Suit are presumed valid. 35 U.S.C. § 282. Moreover, PharmaStem notes that with respect to the reexamined "grandfather" '681 Patent of the patent family of the Patents-In-Suit, the '681 Patent twice passed scrutiny in the Patent and Trademark Office. PharmaStem anticipates that ViaCell will not be able to adduce any new prior art that has not already been considered and reconsidered by the Patent and Trademark Office. *See Transmatic, Inc. v. Gulton Indus., Inc.*, 53 F.3d 1270 (Fed. Cir. 1995)(district court properly granted summary judgment dismissing the accused infringer's invalidity defense because, *inter alia*, the patent claims had "twice passed scrutiny in the PTO, including a reexamination procedure in which [the accused infringer] participated as the requester).

III. PHARMASTEM WILL SUFFER IRREPARABLE HARM ABSENT A PRELIMINARY INJUNCTION.

The Federal Circuit has consistently and repeatedly held that patent infringement gives rise to a presumption of irreparable harm:

> "[I]t is well settled that, because the principal value of a patent is its statutory right to exclude, the nature of the patent grant weighs against holding that monetary damages will always suffice to make the patentee whole. The patent statute provides injunctive relief to preserve the legal interest of the parties against future infringement which may have market effects never fully compensable in money.

Hybritech, 849 F.2d at 1456-57; *see also H.H. Robertson*, 820 F.2d at 390 ("This presumption derives in part from the finite term of the patent grant, for patent expiration is not suspended during litigation, and the passage of time can work irremediable harm."). Accordingly, PharmaStem is entitled to a rebuttable presumption that it would be irreparably harmed if preliminary injunction were not to issue, because it has established a reasonable likelihood of success on the merits. *See Bell & Howell Document Mgmt. Prod. Co. v. Altek Sys.*, 132 F.3d 701, 705 (Fed. Cir. 1997); *see also Jack Guttman, Inc. v. Kapykake Enterprises, Inc.*, 302 F.3d

1352, 1356 (Fed. Cir. 2002)(vacating and remanding denial of preliminary injunction because "a clear showing of likelihood of success on the merits entitles a patentee to a rebuttable presumption of irreparable harm").

Moreover, given the reasonable likelihood—demonstrated herein—of PharmaStem's ultimately prevailing in this lawsuit either at trial or as a matter of law, without preliminary injunctive relief PharmaStem will have no way to recoup losses stemming from the loss of market share that ViaCell obtains while infringing the Patents-In-Suit. PharmaStem currently has sixteen licensees who are in direct competition with ViaCell.[39] These licensee cord blood banks form the royalty base for PharmaStem's income from its cord blood banking intellectual property. There loss of market share, PharmaStem's loss of goodwill in the marketplace if it cannot enforce its patent rights, cannot be quantified in money damages and will be impossible to fully recover.

Finally, when the patent does not have many more years to run, the "equities weigh heavily against the wrongdoer." *H.H. Robertson*, at 391. In this case, one of the Patents-In-Suit expires in approximately three years, while even the most long-lived of the Patents-In-Suit has only approximately five more years to run. In the face of such circumstances, courts have recognized that absent the ability to obtain injunctive relief "the right to exclude granted by the patent would be diminished, and the express purpose of the Constitution, to promote the progress of the useful arts, would be seriously undermined. The patent owner would lack much of the leverage, afforded by the right to exclude, to enjoy the full value of his invention in the market place." *Smith Int'l, Inc. v. Hughes Tool Co.*, 718 F.2d 1573, 1578 (Fed. Cir. 1983). "Without the right to obtain an injunction, the patentees right to exclude would have only a fraction of the value it was intended to have, and would no longer be as great an incentive to engage in the toils of scientific and technological research." *Id.*; *see also PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1566-67 (Fed. Cir. 1996)(affirming grant of preliminary injunction based,

[39] A true and correct copy of a list of PharmaStem's existing licensees is set forth at Appendix C.

in part, on finding that non-movant had not rebutted presumption of irreparable harm in light of finding that movant's market position would be threatened in the absence of injunctive relief). Thus, absent preliminary injunctive relief ViaCell's infringing cord blood banking activities will irreparably harm PharmaStem and its licensees and unjustly diminish PharmaStem's patent rights.

III. THE BALANCE OF HARDSHIPS TIPS IN PHARMASTEM'S FAVOR.

The balance of hardships should be assessed on a sliding scale. *H.H. Robertson*, at 390. To the extent that PharmaStem is able to make a strong showing of likelihood of success on the merits, a lesser showing of hardship is required. *Id.* The reason for the sliding scale is obvious. "One who elects to build a business on a product found to infringe cannot be heard to complain if an injunction against continuing infringement destroys the business so elected." *Windsurfing Int'l, Inc. v. AMF, Inc.*, 782 F.2d 995, 1003, n.12 (Fed. Cir. 1986).

Despite the lower bar for demonstrating hardship warranted by the strength of PharmaStem's likelihood of infringement showing against ViaCell, PharmaStem is suffering greater hardship than ViaCell by any measure. As described above, PharmaStem faces significant hardships, multiplied by the hardship of its sixteen licensees, which will only be compounded absent a preliminary injunction against ViaCell. Moreover, under the terms of the proposed injunction, ViaCell's hardship will be minimized. Under the proposed injunction, ViaCell would still be able to (1) continue to store its existing CBUs and (2) distribute its client's CBUs for transplantation. Thus, while PharmaStem is certainly not indemnifying ViaCell from any damages it may owe to PharmaStem, by a rough estimate derived from ViaCell's own publicized information, the proposed injunction will not stop ViaCell's current cash flow from its annual storage fees of $125 per CBU[40] multiplied by the approximately 60,000 CBUs[41] it stores. Such figures represent an annualized cash flow of approximately $7.5 million. Even if ViaCell's actual annualized cash flow was only half of $7.5 million, it would still most likely be able to

[40] *See* Little Decl., Exh. 9, at page 1.
[41] *See* Little Decl., Exh. 16, at pages 2-3.

easily afford to pay its general, administrative, and operating costs. As a result, ViaCell will be unable to show any cognizable hardship greater than PharmaStem's own arising from the proposed injunction.

IV. THE PUBLIC INTEREST FAVORS AN INJUNCTION.

The present circumstances present no risk that the public interest will be adversely affected by a preliminary injunction. Not only are PharmaStem's sixteen existing licensees ready, willing, and able to meet consumer cord blood banking demand, but PharmaStem's proposed injunction ensures ViaCell's existing clients still have full access to their cord blood units. Through the proposed injunction, PharmaStem seeks only to prevent ViaCell from enrolling new cord blood banking customers while this action is pending.

The public interest is also best served when valid patent rights are upheld and enforced. *See Illinois Tool Works, Inc. v. Grip-Pak, Inc.*, 906 F.2d 679 (Fed. Cir. 1990); *see also Smith*, at 1581 ("public policy favors protection of the rights secured by valid patents"); *Richardson v. Suzuki Motor Co., Ltd.*, 868 F.2d 1226, 1246-47 (Fed. Cir. 1989)("it is contrary to the laws of property, of which the patent law partakes, to deny the patentee's right to exclude others from use of his property"). Indeed, the Patents-In-Suit present an especially compelling case for enforcement, as they have indisputably endowed the medical and scientific arts with an original and new, life-saving, medical technology.

CONCLUSION

For all of the above reasons, PharmaStem respectfully submits that it is entitled to the entry of a preliminary injunction against ViaCell in substantially the same form as the Proposed Preliminary Injunction filed herewith, and for what further and other relief the Court may deem proper or just.

Respectfully submitted,

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Dated: January 7, 2004

CERTIFICATE OF SERVICE

I hereby certify that on this 7th day of January 2005, I have caused a true and accurate copy of the foregoing to be served upon counsel of record as follows:

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